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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/852,845	05/11/2001	Wayne Godfrey	16524.010	7084

28381 7590 12/31/2002

ARNOLD & PORTER
IP DOCKETING DEPARTMENT; RM 1126(b)
555 12TH STREET, N.W.
WASHINGTON, DC 20004-1206

EXAMINER
BELYAVSKYI, MICHAIL A

ART UNIT	PAPER NUMBER
1644	10

DATE MAILED: 12/31/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/852,845	GODFREY ET AL.	
	Examiner	Art Unit	
	Michail A Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 November 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *35 and 59-91* is/are pending in the application.

4a) Of the above claim(s) *73-77* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *35, 59-72 and 78-91* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 11/18/02 (Paper No. 9), is acknowledged.

Claims 35 and 59-91 are pending.

Claims 73-77 stand withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention.

Claims 35, 59-72 and 78-91 are under consideration in the instant application.

2. In view of the amendment, filed 11/18/02 (Paper No. 9) the following rejections remain:

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 35, 59-72, 78, 84, 88, 90 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention essentially for the same reasons set forth in the previous Office Action, paper NO:7, mailed 7/16/02.

5. It is apparent that L 106 antibodies are required to practice the claimed invention. As required elements, they must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If they are not so obtainable or available, the enablement requirements of 35 U.S.C. 112, first paragraph, may be satisfied by a deposit of the pertinent cell lines which produce these antibodies. See 37 CFR 1.801-1.809.

Applicant's arguments, filed 11/18/02 , Paper No. 9 have been fully considered, but have not been found convincing.

Applicant asserts that a Deposit Declaration with an attached copy of the Receipt of an Original Deposit has been enclosed with the Response filed 11/18/02 (Paper No. 9).

However, it is noted that no said Deposit Declaration with an attached copy of the Receipt of an Original Deposit has been received with the Response filed 11/18/02 (Paper No. 9).

Applicant himself acknowledge (see Response filed 11/18/02 , Paper No. 9) that the only listed documents forwarded are:
1. a Petition for Extension of Time;
2. a Response to the Office Action;
3. a return postcard.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112.
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 65, 68 71 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention essentially for the same reasons set forth in the previous Office Action, paper NO:7, mailed 7/16/02.

Claims 65, 68 71 are indefinite in the recitation of "L106 antibody" because its characteristics are not known. The use of " L106 antibody " as the sole means of identifying the claimed antibody and hybridoma renders the claim indefinite because " L106 antibody " is merely a laboratory designation which does not clearly define the claimed product, since different laboratories may use the same laboratory designation s to define completely distinct hybridoma.

Applicant's arguments, filed 11/18/02 , Paper No. 9 have been fully considered, but have not been found convincing.

Applicant asserts that claims have been amended to recite ATCC Accession number.

Contrary to Applicants assertion, the said claims have not been amended.

8. Claims 59 and 62, 79 are rejected under 35 U.S.C.102(b) as being anticipated by Knapp et al. (Leucocyte Typing IV,1989) essentially for the same reasons set forth in the previous Office Action, paper NO:7, mailed 7/16/02.

Knapp et al. teach the same L106 antibody (Table 4, page 391, or Table 1, page 482 in particular).

Applicant's arguments, filed 11/18/02 , Paper No. 9 have been fully considered, but have not been found convincing.

Applicant asserts that there is no way to determine if the antibody designated as L106 is the same as the antibody claimed in the present invention (that is able to bind to ACT-4-h-1) (see page 11 forth paragraph in particular). On the other hand, Applicant asserts that "even if the examiner had established the inherency of the binding of the L106 antibody of Knapp et al., to ACT-4-h-1 this characteristic would not be obvious " (see page 12 forth paragraph in particular).

Since the office does not have a laboratory to test the reference antibodies, it is applicant's burden to show that the reference antibodies do not bind to ACT-4-h-1 or ACT-4 as recited in the claims. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); *In re Fitzgerald et al.*, 205 USPQ 594 (CCPA 1980). In addition, applicant is invited to consider the following decisions based upon generating antibodies. Whether the rejection is based on "inherence" under 35 U.S.C. § 102 or prima facie obviousness under 35 U.S.C. § 103, jointly or alternatively, the burden of proof is the same and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. Examiner properly shifted burden to applicant to establish, through objective evidence, that hybridoma and monoclonal antibody of invention differ in unobvious manner from those of the prior art references. Ex parte Phillips, 28 USPQ2d 1302 (BPAI 1993).

In response to applicant's argument that "even if the examiner had established the inherency of the binding of the L106 antibody of Knapp et al., to ACT-4-h-1 this characteristic would not be obvious". A recitation of the intended use of the claimed invention (that is the ability of L106 antibody to bind to ACT-4-h-1) must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. For example in Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999); the following was noted. "Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art. However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer. " The Court further held that "this same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art". See MPEP 2112.02. Also, see Bristol-Myers Squibb Co. v. Ben Venue Laboratories, Inc. 58 USPQ2d 1508 (CA FC 2001); Ex parte Novitski 26 USPQ 1389 (BPAI 1993); Mehl/Biophile International Corp. V. Milgraum, 52 USPQ2d 1303 (Fed. Cir. 1999); Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999).

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 78 and 80 is rejected under 35 U.S.C. 103(a) as being unpatentable over Knapp et al. (Leucocyte Typing IV,1989) in view of Thorpe et al. (Immunological Rev., 1982) essentially for the same reasons set forth in the previous Office Action, paper NO:7, mailed 7/16/02.

Applicant's arguments, filed 11/18/02 , Paper No. 9 have been fully considered, but have not been found convincing.

Applicant asserts that since Knapp et al. is not an enabling reference, it cannot be combine with other references for a rejection under 35 U.S.C. 103(a).

As has been discussed supra, it is the examiner position that Knapp et al. is an enabling reference, thus it can be combine with other references for a rejection under 35 U.S.C. 103(a).

The claimed invention differs from the Knapp et al. reference teaching only by the recitation of immunotoxin comprising L106 antibody fused to a toxin polypeptide .

Thorpe et al. teach immunotoxin by linking toxins to antibodies in order to attack tumor cells (see entire document, page 119 in particular).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to generate immunotoxin taught by Thorpe et al. using the antibody taught by Knapp et al.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because the antibody could be used to target toxins to tumor cells as taught by Thorpe et al.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expection of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

11. Claims, 35, 60, 61 and 64-72, and 81-91 are rejected under 35 U.S.C. 103(a) as being unpatentable over Knapp et al. (Leucocyte Typing IV,1989) in view of Owens *et al* (J.of Immunol.. Method. 1994) and Bird *et al* (Science,1988) essentially for the same reasons set forth in the previous Office Action, paper NO:7, mailed 7/16/02.

Applicant's arguments, filed 11/18/02 , Paper No. 9 have been fully considered, but have not been found convincing.

Applicant asserts that since Knapp et al. is not an enabling reference, it cannot be combine with other references for a rejection under 35 U.S.C. 103(a). In addition, Applicant asserts that none of the secondary references disclosed or suggest an L106 antibody which specifically binds to ACT-4-h-1.

As has been discussed supra, it is the examiner position that Knapp et al. is an enabling reference, thus it can be combine with other references for a rejection under 35 U.S.C. 103(a).

In addition, Applicants have traversed the primary and the secondary references pointing to the differences between the claims and the disclosure in each reference. Applicant is respectfully reminded that the rejection is under 35 USC103 and that unobviousness cannot be established by attacking the references individually when the rejection is based on the combination of the references. see In re Keller, 642 F.2d 4B, 208 USPQ 871, 882 (CCPA 1981) See MPEP 2145. This applicant has not done, but rather argues the references individually and not their combination. One cannot show non-obviousness by attacking references individually where the rejections are based on a combination of references. In re Young 403 F.2d 759, 150 USPQ 725 (CCPA 1968).

The claimed invention differs from the Knapp et al. reference teaching only by the recitation of a fragment of the L106 antibody (Claims 35 , 60, 81,), heavy chain of L106 antibody, light chain of L106 antibody, Fab fragment antibody, Fab' fragment antibody, $F(ab')_2$ fragment antibody, Fabc fragment antibody, Fv fragment antibody (Claims 61 and 86) and fragment of humanized L106 antibody (Claims 66 and 87).

Owens *et al* teach the modification of murine antibodies such as a chimeric antibody, a single chain antibody, a Fab fragment, a $F(ab')_2$ fragment or a humanized antibody , monoclonal antibody technology including, chimeric, single chain, Fab fragments, and $F(ab')_2$. Owens *et al* further teach humanized antibodies use in therapy of human diseases or disorders, since the human or humanized antibodies are much less likely to induce an immune response. Also, antibody fragments are the reagents of choice for some clinical applications, and the chimeric antibodies offers the ability to mediate antigen-dependent cytotoxicity and complement - dependent cytotoxcity (see the entire document).

Bird *et al* teach a single chain antigen binding proteins composed of an antibody variable light - chain amino acid sequence (V_L) tethered to a variable heavy -chain sequence (V_H) by a designed peptide that links the carboxyle terminus of the V_L sequence to the amino terminus of the V_H sequence. Bird *et al* further teach that the single chain antibodies have significant advantages over monoclonal antibodies in a number of applications such as lower back ground in imaging applications since the single chain antibody lack the Fc portion (see the entire document and page 426, left column, 2nd paragraph in particlular)).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use L106 antibody taught by Knapp et al. to make a fragment of the

L106 antibody; a heavy chain of L106 antibody; a light chain of L106 antibody, a Fab fragment antibody, a Fab' fragment antibody, a $F(ab')_2$ fragment antibody, a Fabc fragment antibody, a Fv fragment antibody, a fragment of humanized L106 antibody, a humanized antibody, a Fab and $F(ab')_2$ fragments taught by Owens *et al.* or as a single chain antibody as taught by the Bird *et al.*

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because the humanized antibodies are much less likely to induce an immune response and because the antibody fragments are the reagents of choice for some clinical applications and the chimaeric antibodies offers the ability to mediate antigen-dependent cytotoxicity and complement-dependent cytotoxcity as taught by Owens *et al.* and because single chain antibodies have significant advantages over monoclonal antibodies in a number of applications such as lower back ground in imaging applications since the single chain antibody lack the Fc portion as taught by Bird *et al.*

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expection of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

12. The following new ground of rejection is necessitated by the amendment filed 11/18/02 (Paper No. 19).

13. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

14. Claims 79-91 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of: a monoclonal antibody and a fragment of said antibody; a humanized antibody and a fragment of said antibody that specifically binds to ACT-4-h-1 of SEQ ID NO:2 .

Applicant is not in possession of : a monoclonal antibody and a fragment of said antibody; a humanized antibody and a fragment of said antibody that specifically binds to *any* ACT-4-h-1 .

The specification fails to described *any* ACT-4-h-1. Applicant has disclosed only one ACT-4-h-1 of SEQ ID NO:2 ; therefore, the skilled artisan cannot envision all the contemplated antibody possibilities broadly recited in the instant claims. Consequently, conception in either case cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. The sequences themselves are required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993).

A description of a genus of antibody may be achieved by means of a recitation of a representative number of antibody, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. Regents of the University of California v. Eli Lilly&Co., 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

15. No claim allowed

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is (703) 308-4232. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Michail Belyavskyi, Ph.D.
Patent Examiner
Technology Center 1600
December 30, 2002

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600